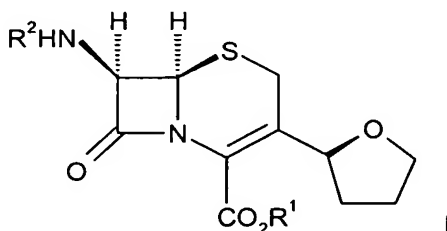
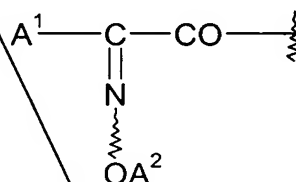


CLAIMS

1. A process for preparing a 3-cyclic-ether-substituted cephalosporin of the formula I:



5 or a pharmaceutically acceptable salt thereof,  
wherein  
the group CO₂R¹ is a carboxylic acid or a carboxylate salt; and  
R² has the formula:

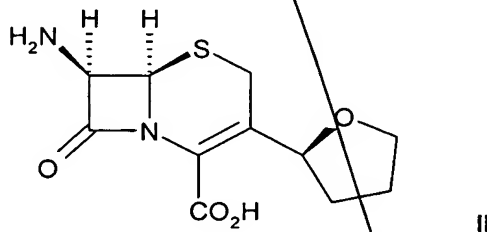


10 wherein

A¹ is selected from the group consisting of C₆-₁₀aryl, C₁-₁₀heteroaryl and C₁-₁₀heterocyclyl;

A² is selected from the group consisting of hydrogen, C₁-₆alkyl, C₃-₁₀cycloalkyl, C₆-₁₀aryl, C₁-₆alkyl(CO)(C₁-₆)alkyl-O-, HO(CO)(C₁-₆)alkyl, mono-(C₆-₁₀aryl)(C₁-₆alkyl),  
15 di-(C₆-₁₀aryl)(C₁-₆alkyl), and tri-(C₆-₁₀aryl)(C₁-₆alkyl);

comprising reacting a compound of formula II:



with a compound of the formula III:



20 wherein

R² is as defined above; and

L is selected from the group consisting of hydroxy, halo, azido, mono(C₁-₆alkyl)carbonate, (C₁-₆alkyl)carboxylate, (C₆-₁₀aryl)carboxylate,

Sub  
A4

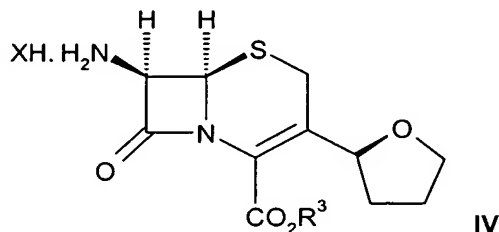
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Sub  
A4

mono-(C<sub>6-10</sub>aryl)(C<sub>1-6</sub>alkyl)carboxylate, di-(C<sub>6-10</sub>aryl)(C<sub>1-6</sub>alkyl)carboxylate,  
di-(C<sub>1-6</sub>alkyl)phosphorothioate, (C<sub>1-6</sub>alkyl)sulfonyl, mono-(C<sub>1-6</sub>alkyl)(C<sub>6-10</sub>aryl)sulfonyl,  
di-(C<sub>1-6</sub>alkyl)(C<sub>6-10</sub>aryl)sulfonyl, (C<sub>1-6</sub>alkyl)-(CO)-S-, cyano-C<sub>1-6</sub>alkoxy, C<sub>6-10</sub>aryloxy,  
3-benzthiazolyloxy, 8-quinolinylloxy and N-oxy-succinimidyl;

- 5 in the presence of a solvent, a base, an optional coupling agent and an optional catalyst.

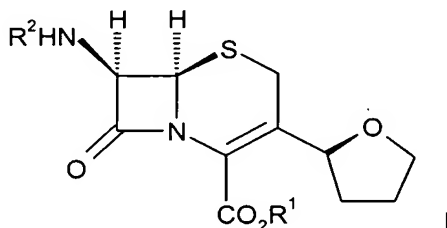
2. The process according to claim 1 further comprising the step of preparing said compound of formula II by reacting a compound of formula IV:



- 10 wherein R<sup>3</sup> is para-nitrobenzyl or allyl; and X is halo;

with a suitable deprotecting agent; in the presence of a solvent.

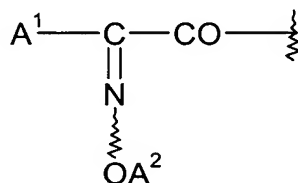
3. A process for preparing a 3-cyclic-ether-substituted cephalosporin of the formula I:



- 15 or a pharmaceutically acceptable salt thereof,

wherein the group CO<sub>2</sub>R<sup>1</sup> is a carboxylic acid or a carboxylate salt; and

R<sup>2</sup> has the formula:

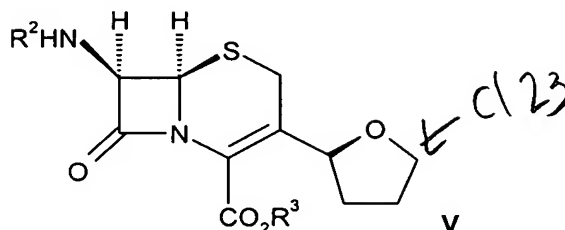


- 20 wherein A<sup>1</sup> is selected from the group consisting of C<sub>6-10</sub>aryl, C<sub>1-10</sub>heteroaryl and C<sub>1-10</sub>heterocyclyl;

A<sup>2</sup> is selected from the group consisting of hydrogen, C<sub>1-6</sub>alkyl, C<sub>3-10</sub>cycloalkyl, C<sub>6-10</sub>aryl, C<sub>1-6</sub>alkyl(CO)(C<sub>1-6</sub>alkyl)-O-, HO(CO)(C<sub>1-6</sub>alkyl), mono-(C<sub>6-10</sub>aryl)(C<sub>1-6</sub>alkyl), di-(C<sub>6-10</sub>aryl)(C<sub>1-6</sub>alkyl) and tri-(C<sub>6-10</sub>aryl)(C<sub>1-6</sub>alkyl);

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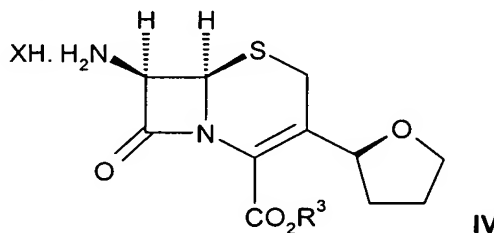
comprising reacting a compound of formula V:



wherein R<sup>2</sup> is as defined above; and R<sup>3</sup> is para-nitrobenzyl or allyl;

with a suitable deprotecting agent in the presence of a solvent.

5            4.        The process according to claim 3 further comprising preparing said compound of formula V by reacting a compound of formula IV:

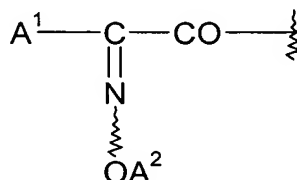


wherein R<sup>3</sup> is para-nitrobenzyl or allyl; and X is halo;

with a compound of the formula III:

10  $R^2L$  III;

wherein R<sup>2</sup> has the formula:



wherein  $A^1$  is selected from the group consisting of  $C_{6-10}$ aryl,  $C_{1-10}$ heteroaryl and  $C_{1-10}$ heterocyclyl;

15 A<sup>2</sup> is selected from the group consisting of hydrogen, C<sub>1-6</sub>alkyl, C<sub>3-10</sub>cycloalkyl, C<sub>6-10</sub>aryl, C<sub>1-6</sub>alkyl(CO)(C<sub>1-6</sub>)alkyl-O-, HO(CO)(C<sub>1-6</sub>)alkyl, mono-(C<sub>6-10</sub>aryl)(C<sub>1-6</sub>alkyl), di-(C<sub>6-10</sub>aryl)(C<sub>1-6</sub>alkyl) and tri-(C<sub>6-10</sub>aryl)(C<sub>1-6</sub>alkyl); and

L is selected from the group consisting of hydroxy, halo, azido, mono(C<sub>1-6</sub>alkyl)carbonate, (C<sub>1-6</sub>alkyl)carboxylate, (C<sub>6-10</sub>aryl)carboxylate, mono-(C<sub>6-10</sub>aryl)(C<sub>1-6</sub>alkyl)carboxylate, di-(C<sub>6-10</sub>aryl)(C<sub>1-6</sub>alkyl)carboxylate, di(C<sub>1-6</sub>alkyl)phosphorothioate, (C<sub>1-6</sub>alkyl)sulfonyl, mono-(C<sub>1-6</sub>alkyl)(C<sub>6-10</sub>aryl)sulfonyl, di-(C<sub>1-6</sub>alkyl)(C<sub>6-10</sub>aryl)sulfonyl, (C<sub>1-6</sub>alkyl)-(CO)-S-, cyano-C<sub>1-6</sub>alkoxy, C<sub>6-10</sub>aryloxy, 3-benzthiazolyloxy, 8-quinolinyloxy and N-oxy-succinimidyl;

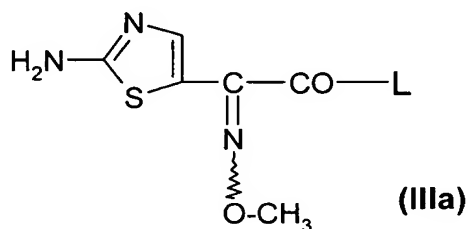
in the presence of a solvent.

5. The process according to claim 1, wherein said A<sup>1</sup> moiety of said R<sup>2</sup> is C<sub>1-10</sub>heteroaryl selected from the group consisting of furyl, thienyl, pyridyl, aminothiazolyl and aminothiadiazolyl, wherein said amino moiety of said aminothiazolyl or aminothiadiazolyl is optionally protected.

6. A process according to claim 1, wherein said A<sup>2</sup> moiety of said R<sup>2</sup> is C<sub>1-6</sub>alkyl.

7. A process according to claim 1, wherein L of said compound of the formula III is selected from the group consisting of halo, methanesulfonyl, diethylphosphorothioate and 3-benzthiazolyloxy.

8. A process according to claim 1, wherein said compound of formula III has a formula IIIa:



and wherein L is selected from the group consisting of halo, methanesulfonyl, diethylphosphorothioate and 3-benzthiazolyloxy.

9. A process according to claim 1, wherein said solvent is water, acetone, tetrahydrofuran, ethyl acetate, dimethylacetamide, dimethylformamide, acetonitrile, methylene chloride, 1,2-dichloroethane or mixtures thereof.

10. A process according to claim 1, wherein said solvent is water, acetone, or mixtures thereof.

11. A process according to claim 1, wherein a catalyst is used.

12. A process according to claim 11 wherein said catalyst is a Lewis acid catalyst selected from the group consisting of boron trihalide and aluminum halide.

13. A process according to claim 1 wherein said base is diisopropylethylamine or sodium hydroxide.

14. A process according to claim 1, wherein said coupling agent is selected from the group consisting of N,N'-diethylcarbodiimide, N,N'-dipropyl carbodiimide, N,N'-diisopropylcarbodiimide, N,N'-dicyclohexylcarbodiimide, N-ethyl-N'-[3-(dimethylamino)propyl]carbodiimide, N,N'-carbonyldiimidazole and N,N'-carbonyldithiazole.

15. A process according to claim 1, wherein said coupling agent is N,N'-dicyclohexylcarbodiimide.

16. A process according to claim 1, wherein said X is chloro.

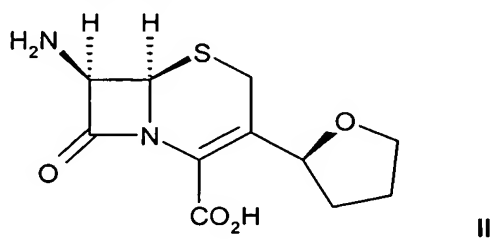
17. A process according to claim 2, wherein said  $R^3$  is para-nitrobenzyl and said suitable deprotecting agent is sodium dithionite or a catalytic hydrogenating agent.

18. A process according to claim 2, wherein said  $R^3$  is allyl and said suitable deprotecting agent is tetrakis triphenylphosphine palladium (0).

5 19. A process according to claim 17, wherein said solvent is acetone, water, tetrahydrofuran or mixtures thereof.

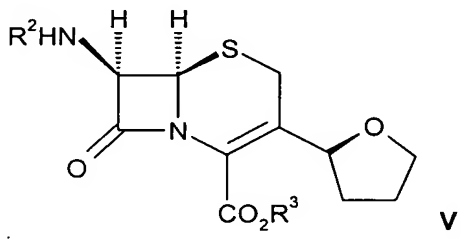
20. A process according to claim 4, wherein said solvent is methylene chloride, tetrahydrofuran or mixtures thereof.

21. A compound of formula II:



22. The compound according to claim 21 wherein said compound of the formula II has an enantiomeric or diastereomeric purity of 96% to 100%.

23. A compound of formula V:



15 wherein  $R^2$  is acyl; and  $R^3$  is para-nitrobenzyl or allyl.

24. The compound according to claim 23 wherein said compound of the formula V has an enantiomeric or diastereomeric purity of 96% to 100%.